

# Long-term benefits of coronary bypass surgery: Are the gains for women less than for men?

Viola Vaccarino, MD, PhD<sup>a</sup>  
Colleen Gorman Koch, MD<sup>b</sup>

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1704, 2032, and 2044.

**T**he issue of whether there are disparities in the outcome of coronary revascularization between women and men, in particular coronary artery bypass graft (CABG) surgery, has been the object of intense debate in the past 10 to 15 years. Studies have disagreed on whether the risks and benefits resulting from CABG surgery differ between women and men. Indeed, few areas of clinical research have been more controversial than this. Overall, clinicians are left with the suspicion that CABG poses special risks in women or is less effective in this group. This fact may discourage prompt referral of women for CABG and lead to gender-related disparities in referral, another area of major debate.<sup>1,2</sup> In turn, a later referral for CABG may contribute to higher operative risk and fewer long-term benefits if women are referred when their disease is more advanced and/or their comorbidity burden worse. Therefore, it is necessary to come soon to a consensus on whether CABG surgery is a beneficial procedure in women, at least to the same extent as it is in men.

A major reason why this question is very difficult to resolve is that major randomized trials of the efficacy of CABG surgery compared with medical therapy have been conducted almost exclusively in men.<sup>3</sup> Most of the trials comparing CABG with percutaneous transluminal coronary angioplasty also have focused on men.<sup>4</sup> Currently, more than 150,000 CABG procedures per year are performed in women in the United States, or almost one third of the total,<sup>5</sup> and the number of CABG procedures performed on women is rapidly increasing, in part due to the gradual aging of the surgical population.<sup>6,7</sup> However, there is no clinical trial evidence supporting the efficacy of this procedure in women. Since CABG has become, nonetheless, part of the standard of care for the treatment of all patients with coronary heart disease, including women, research studies of CABG in women commonly use men as the control group, an approach that is logical but methodologically problematic, as highlighted in previous editorials of this series. This approach tells us whether women benefit from CABG surgery to the same extent as men do, assuming that the comparison between women and men is not biased, but it does not tell us whether women who undergo CABG fare better than women who do not.

## Do Long-Term Benefits of CABG Surgery Differ Between Women and Men?

### Quality of Life

Since CABG yields only a small absolute survival benefit relative to medical therapy, and only in selected subgroups of patients,<sup>3</sup> the main indication for this procedure, in both men and women, is the obtainment of symptom relief and the long-term improvement in function and quality of life. Consequently, patient-centered outcomes such as physical functioning, symptoms, quality of life, and patient satisfaction represent important outcome measurements after surgical interventions. Although studies have not been entirely consistent, in general, the long-term results in terms of symptom status, functioning, and quality of life after CABG surgery tend to be less satisfactory in women than in men. Women have less relief of angina, more dyspnea, and lower functional status in postoperative long-term

From the Department of Medicine, Division of Cardiology, Emory University School of Medicine,<sup>a</sup> Atlanta, Ga, and the Cleveland Clinic Foundation, Department of Cardiothoracic Anesthesia,<sup>b</sup> Cleveland, Ohio.

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Address for reprints: Viola Vaccarino, MD, PhD, Department of Medicine, Division of Cardiology, Emory University School of Medicine, 1256 Briarcliff Rd, Suite 1 N, Atlanta, GA 30306 (E-mail: [lvaccar@emory.edu](mailto:lvaccar@emory.edu)).

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follow-up studies,<sup>7-14</sup> even when their baseline functional status is taken into account.<sup>10,14</sup>

### Long-Term Survival

Despite women's higher rate of perioperative complications, lower symptom relief, and lower patency rate after CABG, long-term survival does not differ between women and men.<sup>15-18</sup> In some studies, the survival of women was even better than men after adjusting for other risk factors.<sup>7</sup> In part, the improved survival of women in the long term may reflect the better life expectancy of women, which may prevail with prolonged follow-up. However, women may not catch up completely to their expected level of survival advantage compared with men, even if observed for a long time after CABG. When the long-term mortality in men and women after CABG is compared with the expected mortality based on the normal population of same age and sex, both male and female CABG patients have higher mortality than population controls. However, in female patients who have had CABG this increased risk is about twice as high as in men, indicating a substantial narrowing of women's survival advantage.<sup>17</sup> A similar phenomenon has been observed after acute myocardial infarction.<sup>19</sup>

### Role of Procedural Factors

Why do women have fewer functional gains and less symptom relief than men after CABG surgery? Women have been shown to receive less complete revascularization<sup>8</sup> and have higher graft occlusion rates<sup>9,13,20,21</sup> than men after CABG, although these differences seem to be decreasing in recent years.<sup>22</sup> These effects have been attributed to women's smaller coronary arteries, which pose technical difficulties, limit graft flow, and predispose to reocclusion.<sup>23,24</sup> Smaller arteries may also be less suitable for repeat revascularization. If CABG surgery yields less complete revascularization or a higher rate of graft failure in women than in men, this might result in less symptom relief and lower functional status in women. Other procedural factors, such as fewer grafts and underuse of the left internal thoracic artery in women, may also be associated with a greater incidence of postoperative angina.

### Role of Patient Characteristics

It is clear that women and men referred for CABG surgery represent two very different patient groups. Several investigations<sup>10,25-29</sup> have consistently described remarkable differences in the demographic, medical, and psychosocial profile of men and women referred for CABG. Women undergoing CABG are older, less educated, and have more severe angina and congestive heart failure, lower functional status, and higher levels of depressive symptoms. Few studies had information on all these factors. Even if all these

characteristics are measured, the possibility of residual or unknown confounding remains.

The presence of such marked differences in age, risk factors, and health status at the time of CABG between women and men raises yet another potential issue to consider. Some authors have suspected that these differences may be due to a later referral of women than of men.<sup>1,2</sup> If indeed there is a different threshold for referral to CABG surgery in women and in men, the gender comparisons may be biased. Paradoxically, despite being more symptomatic, women referred for CABG have less extensive coronary artery disease than men as determined by coronary angiographic results.<sup>8,9,24,30,31</sup> Although this finding raises interesting questions about why women have a more severe presentation in the face of less severe coronary narrowing, it certainly challenges the notion of a delayed referral of women.

The different social roles and social resources of women and men might also play a role in the outcome differences between women and men after CABG.<sup>32</sup> Women try to quickly regain their responsibilities in home management and care giving after a coronary event<sup>33</sup> and tend to resume household activities early during recovery. Therefore, women may experience greater disruptions on returning home after surgery than men because they feel the pressure of resuming their family role. Notably, home management is a functional area in which disparities between men and women are greatest during recovery after CABG.<sup>32,34</sup> These facts may be exacerbated by women's higher rate of depression and may increase women's propensity to experience symptoms and disability after surgery.

### Role of Management Strategies After CABG

#### Pharmacologic Management

Studies have clearly pointed out the beneficial effects of preoperative and postoperative aspirin<sup>35,36</sup> and preoperative  $\beta$ -blocker use<sup>37</sup> on mortality after CABG. The American College of Cardiology and the American Heart Association have produced jointly detailed clinical guidelines for the in-hospital and post-hospital care of patients undergoing CABG surgery.<sup>38</sup> Recommended management strategies to maximize postoperative benefit include antiplatelet therapy, which reduces the risk of vein graft closure, pharmacologic treatment of hyperlipidemia, smoking cessation, and cardiac rehabilitation.

Studies of patients having an acute myocardial infarction have reported a lower use of recommended treatments in women than in men,<sup>39,40</sup> but little is known whether there are gender differences in the preoperative or postoperative use of recommended pharmacologic regimens in patients undergoing CABG. Some studies did report a lower use of aspirin either preoperatively or early postoperatively than in men,<sup>35,36,41,42</sup> but these differences were unadjusted; there-

fore, they may have been due to the older age of the women or other factors. If there are differences in the management of patients after CABG according to gender, these differences could play a role in the less satisfactory response of CABG for the improvement of quality of life in women.

### Cardiac Rehabilitation

A management strategy after CABG for which gender differences have been more thoroughly examined is cardiac rehabilitation. Cardiac rehabilitation has been shown to increase exercise capacity and improve cardiovascular risk profile after CABG surgery, but only 10% to 40% of patients enroll in cardiac rehabilitation programs.<sup>43-45</sup> Women have consistently shown lower enrollment rates than men,<sup>43,44</sup> despite the fact that they benefit from rehabilitation as much as men.<sup>44,46-48</sup> The low attendance of women compared with men appears to be the result of both lower physician referral<sup>43,49,50</sup> and lower participation of women.<sup>50</sup>

It is widely debated whether the gender differences in referral to rehabilitation are related to gender bias or to differences in women's and men's health status and psychosocial characteristics. Factors that have been associated with lower enrollment in cardiac rehabilitation include psychosocial characteristics, such as low education,<sup>51,52</sup> social isolation,<sup>53-57</sup> being unemployed,<sup>51,52</sup> being unmarried,<sup>51,52,55,58</sup> depression, anxiety, and low self-esteem,<sup>53,55</sup> all factors that tend to be more common in women than in men after CABG. Additional important determinants of lower participation are cardiovascular risk factors and comorbidities,<sup>51,52,55,59,60</sup> which are also more common among women. These factors may influence both the patient's and the physician's decision about participation in rehabilitation programs. The level of physical function in the early recovery period after CABG is one of the most powerful predictors of enrollment in rehabilitation,<sup>44,61</sup> and the lower the function, the lower the enrollment.<sup>61</sup> Indeed, differences in physical function may play a major role in gender differences in rehabilitation after CABG.<sup>62</sup> These differences in care, however, do not seem justified. Rehabilitation programs can be fitted for the needs of individual patients, even those with severely impaired physical function. In addition, even mild rehabilitation intervention improves survival and health outcomes,<sup>63</sup> and patients with lower physical function are the most likely to benefit from it.<sup>64,65</sup>

### Are the Differences Beginning to Disappear?

Despite the fact that patients referred for CABG have been increasingly older and sicker in recent years, the in-hospital mortality rates are declining.<sup>6</sup> An encouraging fact is that this is true particularly among women.<sup>31</sup> Although data on time trends on long-term outcomes are not available, these

statistics are indeed reassuring that CABG outcomes are improving in women. It is likely that technical advancements in surgical and myocardial protection techniques, such as the increasing use of off-pump procedures, the increasing use of internal thoracic artery grafts, and the ability to successfully operate on small arteries, have contributed and will likely continue to contribute to the narrowing of the gender gap in the risks and benefits of CABG surgery.<sup>31</sup> Additional efforts, however, will be required to maximize the long-term physical and psychological gains after CABG in women. There is the need of further exploration of the reasons for the disproportionate severity of symptoms and risk factors in relation to the angiographic extent of disease in women compared with men, because this may shed light on whether special efforts should be directed toward operating on women earlier in their clinical course. In addition, given the peculiar characteristics of female patients having CABG in terms of their cardiovascular risk profile, more investigation should be devoted toward elucidating whether there are specific subgroups of women who may benefit from surgery the most. It will also be very important to clarify the impact of the psychosocial environment on the successful recovery of women, as well as maximize women's postoperative quality of care, including participation in cardiac rehabilitation.

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